Efficacy of Selective Transarterial Chemotherapy Using a Port System for Angiosarcomas of the Face and Scalp

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Summary

Angiosarcoma is a rare, highly malignant tumor with a poor clinical outcome. From January 2004 to September 2005, we advocated transarterial chemotherapy using a port system for four patients with angiosarcomas of the face and scalp. A heparin coated ANTHRON P-U catheter was introduced into the feeding artery. The proximal part of the P-U catheter was connected to the port system and buried in subcutaneous tissue. The amount of chemotherapeutic drug applied using the port system was almost the same as the conventional intravenous dose. Paclitaxel was the standard agent, at 50-100mg/ diluted in 15-30 ml of physiological saline fluid slowly injected over 0.5-1 hour. For immunotherapy where appropriate, r-IL2 was mainly used at a dose of 70.000U/ diluted in 5ml of physiological saline fluid injected into the port system over 30 seconds. This was continued for two to three weeks (five days/week) until recognition of a disappearance of the tumor. Macroscopic size reduction of the tumor was achieved in three out of the four cases. One case could not be evaluated because of eruptions induced by immunotherapy. Unfortunately two patients died after placement of port system, but the other two are still alive and are enjoying useful lives. Transarterial infusion chemotherapy using such a port system may be particularly effective for angiosarcoma in the early stages because small lesions with limited invasion mean a small territory of blood supply to be covered, and useful life was possible because the port system embedded in subcutaneous tissue allows treatment in an out-patient clinic.

Introduction

Angiosarcomas often occur on the face and scalp and are associated with a poor clinical outcome [1]. One catastrophic event is very early metastasis to the pleura, which can result in massive bleeding into the pleural cavity and aggravate the general clinical condition. Various kinds of treatment have been applied but satisfactory results have not been achieved [2,3]. The present study discusses the efficacy of selective transarterial infusion chemotherapy using a port system buried in subcutaneous tissue for angiosarcomas. Chemotherapy and immunotherapy were continued for two to three weeks (five days/week) until recognition of a disappearance of the tumor. Chemotherapy using the port system was then performed on an outpatient basis.

Materials and Methods

From January 2004 to September 2005, we advocated transarterial chemotherapy using a port system for four patients with angiosarcomas of the face and scalp, all of whom had re-

sisted other treatments. Three of the patients were male and one female, with an age range from 48 to 62 years (average: 57 years). Two had a history of craniofacial injury to the area in which the tumor originated. All the tumors showed immediate local re-growth resistant to conventional chemotherapy which was combined with surgical removal in two patients, and immunotherapy and radiation in two patients (table 1).

Conventional carotid angiography via the femoral artery was initially performed to define feeding arteries for the tumors. A second, J-shaped incision was applied to the supraclavicular region followed by demarcation of subcutaneous tissue. Puncture using a 19G-elaster into the external carotid artery or the common carotid artery was achieved under two-dimensional road mapping. Initially, a short 4Fr sheath (7 cm) was placed into the external carotid artery via direct puncture approach to the common carotid artery or external carotid artery, thereafter a heparin coated ANTHRON 2.7F/ 5.0Fr P-U catheter (TORAY co. Ltd, Japan), which was prepared for 4F sheath by cutting the proximal portion, preceded by microguide wire, was introduced into the feeding artery under road mapping. After test injection of contrast medium to define no reflux to the internal carotid system, the proximal part of the P-U catheter was connected to the port system and buried in subcutaneous tissue after final confirmation of the location by angiography. The amount of chemotherapeutic drug applied using the port system was almost the same as the conventional intravenous dose. Paclitaxel was the standard agent, at 50-100mg/ diluted in 15-30 ml of physiological saline fluid slowly injected over 0.5-1 hour. For immunotherapy where appropriate, recombinant interleukin 2 (r-IL2) was mainly used, at a dose of 70.000U/ diluted in 5 ml of physiological saline fluid injected into the port system over 30 seconds. This was continued for two to three weeks (five days/week) until disappearance of the tumor. Chemotherapy using the port system was then performed on an outpatient basis.

Results

Macroscopic size reduction of the tumor was achieved in three out of the four cases. One case could not be evaluated because of eruptions induced by immunotherapy. Unfortunately two patients died after the placement of port system, but the other two patients are still alive

Table **The summary of our four angiosarcoma cases treated by trans-arterial infusion chemotherapy using port system.**

case	Age/ Sex	Causes	Treatments	Feeding arteries	Port placement	Time until placement from the onset (month)	Term of placement (month)	Tumor size reduction	Outcome (survival time month)
1	59/M	Injury	Radiation Chemotherapy	1) Rt IMA, STA Bifurcation 2) Lt STA	Rt chest Lt chest	18M	3.3M 2.5M	+	Dead (22M)
2	49/M	Injury	Surgical Removal Immunotherapy Chemotherapy Radiation	1) Rt OA 2) Rt OA	Rt Supraclavicular Fossa Rt forearm	13M	2.1M 7.2M	+	Dead 29M
3	59/F	Injury	Chemotherapy Immunotherapy Radiation	Rt STA	Rt Supraclavicular Fossa	16M	5.7M	Undetermined	Survaival (31M)
4	61/M	None	Chemotherapy Surgical Removal	Rt IMA, STA Bifurcation	Rt Supraclavicular Fossa	10M	6.3M	+	Survaival (19M)

IMA: internal maxillary artery, STA: superficial temporal artery, OA; occipital artery
Survival time: survival time from the onset

and are enjoying useful lives. The cause of death was hemothorax and tumor invasion. The survival term in the two deceased patients was 22 months and 29 months (average: 25.5 months) after onset. The other two patients are still alive after 31 months and 19 months (average: 25 months).

The targeted vessels for port system delivery were the superficial temporal artery (STA) in three cases, the occipital artery (OA) in two and the internal maxillary artery (IMA) in one. A total of six procedures were applied for the four patients. All procedures were successfully performed without major complications, but in two the port system needed to be removed, one because of drug leakage and fat necrosis around the port system (two months after placement) and the other due to radiation necrosis (5.6 months after placement). The others could be utilized for 2.5 months and six months (average: 4.8 months) and no obstruction of the port system was encountered.

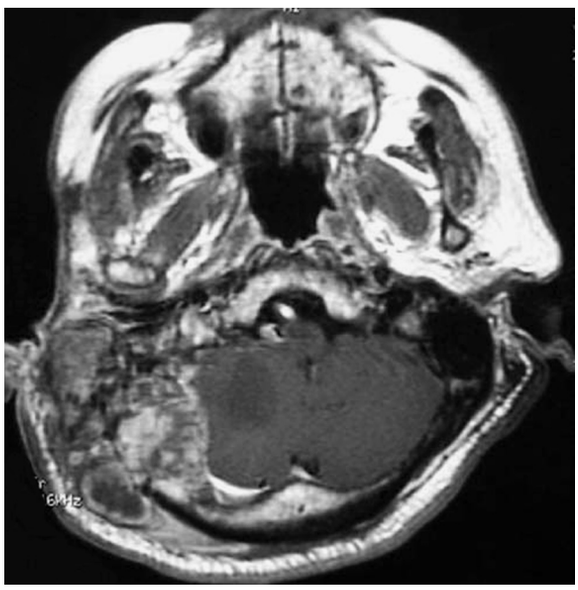

Figure 1 T1-weighted MR image with gadolinium enhancement showing a lesion with irregular enhancement located in the right posterior fossa destroying the bone structure.

Representive Case

Twenty-five years before, a 49-year-old man had a head injury mainly to the right posterior auricular portion resulting in development of a subcutaneous nodule. In July 2001, the size of the nodule immediately increased over two months was operated and was diagnosed as angiosarcoma defined by histological examination. One month after the operation, local tumor recurrence developed with metastasis to the right parotid gland and around the right cervical lymph nodes. One month later, the patient was transported and admitted to our hospital for treatment. Initially, 80 Gray of electron therapy and 40 Gray of X ray combined with chemotherapy (docetaxcel 40 mg droplet in to the venous rout per two weeks) resulted in tumor resolution transiently. However, in May 2002 local recurrence invading the skull was evident on follow-up MRI. The cerebellar symptoms and unconsciousness developed and gradually worsened. Adding radiation therapy of 40 Gray and super-selective intra-arterial chemotherapy from the port system embedded in the subcutaneous tissue were attempted. The right external carotid angiogram showed a lucent tumor stain supplied by the right occipital artery (figure 2). A 2.7/5.0F of ANTHRON PU-catheter (Teijin, Co. Japan) (figure 3A) was super-selectively placed into the right occipital artery and was connected with the CELSITE PORT (figure 3B) embedded in the subcutaneous tissue of the supraclavicular portion. Transarterial chemotherapy using mitoxantrone 14mg/m^2 and paclitaxel 100mg/m^2 from

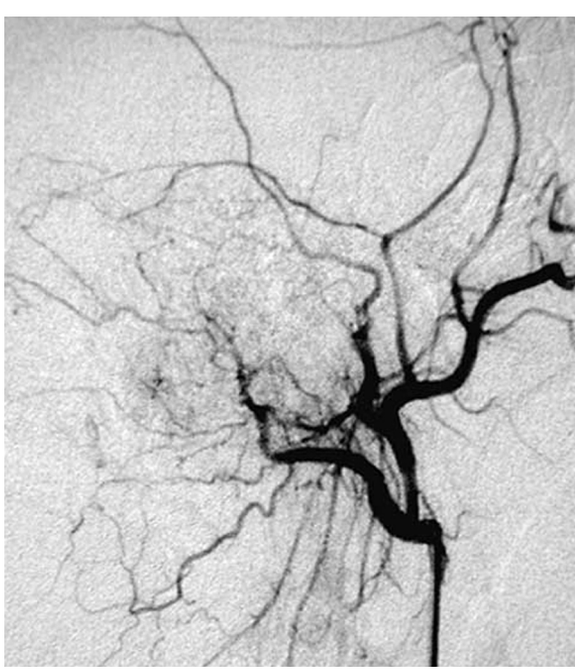

Figure 2 Right external carotid angiogram showing a lucent stain distributed by the occipital artery.

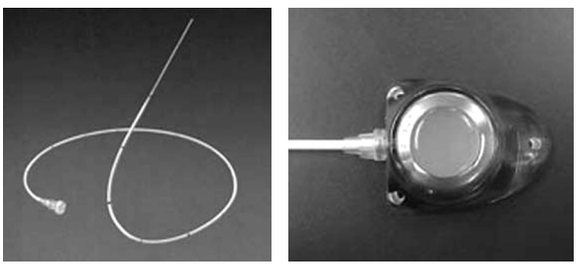

Figure 3 A) ANTHRON 2.7F/5F P-U catheter 90 cm tapering type (TORAY co. Ltd, Japan). B) P-U CELSITE PORT.

the CELSITE PORT system started and continued resulted in recovery of the consciousness one month later but mild bone marrow suppression developed. Three months after the treatment, MRI showed a remarkable size reduction of the tumor with necrosis (figure 5) resulting in social rehabilitation and a valuable life. Intermittent chemotherapy with docetaxil 40-80 mg/m^2 were given intravenously for two weeks at the outpatient clinic. Five months later after discharge, the tumor showed regrowth and the patient was re-admitted to our hospital. Revision of the port system was performed as P-U catheter placed into the right occipital artery via the right brachial artery and CELSITE PORT in the right brachial portion. Retransarterial selective chemotherapy via the port system produced tumor necrosis resulting in bleeding from the right ear. Transarterial chemotherapy via the port system was stopped. Twenty-nine months later the patient was died from brain herniation.

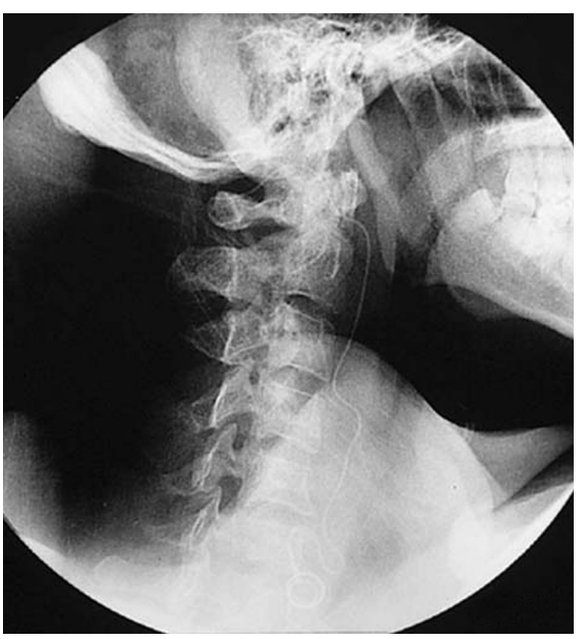

Figure 4 Plain cervical X ray showing an ANTHRON P-U catheter.

Discussion

Angiosarcomas are rare lesions thought to originate from endothelial cells. They account for about 2% of soft tissue tumors and 0.02% of all malignancies. About 60% of angiosarcomas occur in superficial connective tissue and almost half arise in the craniofacial region1. The poor prognosis is due to early growth, early metastasis and high recurrence rate. Rates for five year survival are reported to be 10-35%[3].

For early stage angiosarcomas, immunotherapy using r-IL2 combined with surgery is generally recommended. For late stage disease, chemotherapy combined with radiation has been widely used[2,4]. The biological characteristics need to be taken into consideration for treatment and for craniofacial lesions microvascular direct connections with feeding arteries makes for relatively easy introduction of the drug into tumor vessels. Recently, selective trans-arterial infusion chemotherapy[5] and/or immunotherapy using r-IL2[2] via a port system has been reported to be effective for otherwise untreatable angiosarcomas. However, the details of the operative procedure in account of the port system were not mentioned and are reported here in detail. The main advantage of transarterial chemotherapy using the port system is that it can establish a high concentration of the drug in tumor vessels. The other advantage is that the drug dose may be diminished to minimize the side effects for patients but still maintain an adequate concentration in tumor vessels. In the present small series of patients, useful life was possible because the port system embedded in subcutaneous tissue allows treatment in an outpatient clinic. Transarterial infusion chemotherapy using such a port system may be particularly effective for angiosarcoma in the early stages because small lesions with limited invasion mean a small territory of blood supply to be covered. Another advantage of the port system is that repeated injection of the drug can be performed in an outpatient clinic for recurrence of the tumor resulting in continuous useful life.

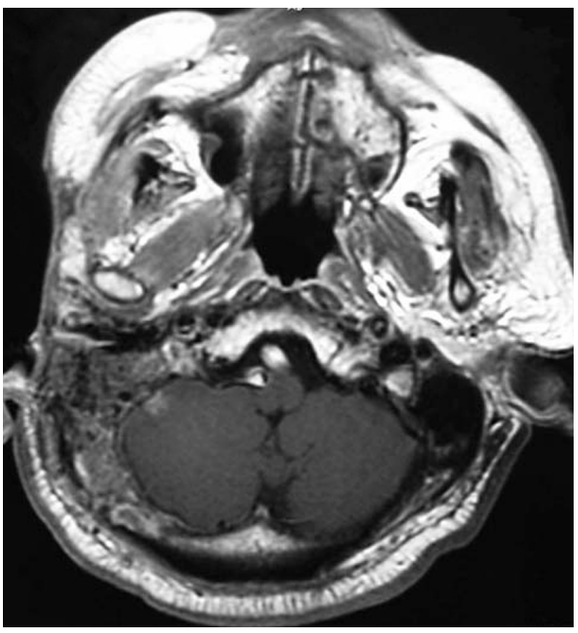

Figure 5 T1-weighted MR image with gadolinium enhancement three months after transarterial chemotherapy using the port system showing a disappearance of the lesion.

The major disadvantage of the port system is the invasive nature of the tumor and the need for superselective angiography under road mapping using digital subtraction angiography for implantation. Direct puncture of the carotid artery may introduce cervical subcutaneous hematomas, which can compress the trachea. Introduction of the catheter may also produce embolic complications and therefore use of an ANTHRON catheter with a coating of heparin is recommended. Furthermore, repeated transarterial infusion chemotherapy sometimes induces obstructions of the feeding artery and this occurred in two out of six procedures in the present series. A high concentration of the drug might also induce vasospasm and result in obstruction of the feeding artery so that attention must be paid to the dose and rate of infusion. If some resistance occurs during injection, angiography should be performed for clarification. In this series, one patient suffered fat necrosis around the port system caused by leakage of the drug and therefore a large size port system is recommended to avoid missed puncture.

Conclusions

Transarterial infusion chemotherapy using the port system will be an ultimate treatment for angiosarcoma in early stages because small lesions with limited invasion mean a small territory of blood supply to be covered.

Technically, transarterial infusion chemotherapy using such a port system resulted in useful life for the patients with a poor outcome neoplasm because the port system embedded in subcutaneous tissue allows treatment in an outpatient clinic.

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